Comparison of Estimated PCB-153 Concentrations in Human Milk Using Various Pharmacokinetic Models

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~~Fish consumption can be a significant source of lipophilic chemicals~~~~contaminants that concentrate in human milk.~~ Risk to infants from consuming ~~contaminated~~ human milk contaminated with lipophilic chemicals has long been overlooked in the risk assessment process. Typically, risk assessors use~~estimate doses of lipophilic contaminants based on their~~ measured chemical concentrations in media of concern. However, ~~The medium of~~ human milk is often difficult to sample for chemical~~contaminant~~ concentrations. Therefore, it is desirable to have models that predict chemical~~contaminant~~ levels in human milk and subsequent average daily doses to the nursing infant (ADDi). ~~Researchers have developed several of these models. The aim of this study was to~~ We compared adaptations of three published models in an effort to help risk assessors and public health practitioners choose an appropriate method to estimate risk to infants via the ~~human~~ milk exposure pathway. The ~~three~~ models chosen for comparison were-: -1) a classic single-compartment ~~first order kinetic~~ model ~~(based on a modification of Smith [Risk Anal. 1987 7:347-353])~~ consisting of a mass-transfer algorithm that calculates a maternal body burden from maternal average daily dose (ADDm), 2) a 3-compartment physiologically-based pharmacokinetic (PBPK) model, ~~based on a model developed by Redding et al. [Environ. Health Perspect. 2008 116: 1629-1634],~~ and 3) a second PBPK model with 8 compartments ~~developed by Verner et al. [Environ. Health Perspect. 2009 117:481-487]~~. The models were compared by running two sets of simulations in each model using the polychlorinated biphenyl congener 153 (PCB-153), a widespread lipophilic environmental contaminant relevant to human health. The first set of simulations used a back-calculated ADDm as a starting point. This ADDm was calculated using the 8-compartment PBPK model based on PCB-153 blood concentrations measured in a human population. From this derived ADDm, the ~~three~~ models simulated both the milk concentration and ADDi. The estimated milk concentrations were then compared to observed concentrations. The second set of simulations used an ADDm derived for PCB-153 assuming consumption of contaminated fish. ~~We then compared the human milk concentrations and ADDi resulting from simulations across the three models.~~ ~~The~~All 3 model results were similar to within a factor of 2. In all cases the classic ~~pharmacokinetic~~ single compartment model produced the highest estimates of PCB-153 concentration in human milk and ADDi. Our results indicate that the simplest model studied may be~~will be used to recommend an~~ appropriate

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~~model~~ for risk assessors and public health practitioners to use for predicting the ADDi for lipophilic environmental contaminants.